

PATENT COOPERATION TREATY

10/541182
REC'D 02 OCT 2005
WIPOFrom the
INTERNATIONAL SEARCHING AUTHORITYTo:
DAVID S. RESNICK
NIXON PEABODY LLP
100 SUMMER STREET
BOSTON, MA 02110-2131

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

| | | |
|---|--|---|
| Date of mailing (day/month/year) | | 31 OCT 2005 |
| Applicant's or agent's file reference | | FOR FURTHER ACTION See paragraph 2 below |
| 700355053461 | | |
| International application No. | International filing date (day/month/year) | Priority date (day/month/year) |
| PCT/US04/00255 | 07 January 2004 (07.01.2004) | 07 January 2003 (07.01.2003) |
| International Patent Classification (IPC) or both national classification and IPC | | |
| IPC(7): B32B 27/04; C12N 5/00, 5/02 and US Cl.: 424/423; 435/325, 395; 442/128 | | |
| Applicant | | |
| TUFTS UNIVERSITY | | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|--|--|
| Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer Dr. Kailash C. Srivastava <i>Maria J. Watson</i> for Telephone No. 703-308-0196 |
|--|--|

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | |
|---|---|---|
| Applicant's or agent's file reference 700355053461 | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/US2004/000255 | International filing date (<i>day/month/year</i>) 07 January 2004 (07.01.2004) | Priority date (<i>day/month/year</i>) 07 January 2003 (07.01.2003)] |
| International Patent Classification (IPC) or national classification and IPC 7 B32B 27/04, C12N 5/00, 5/02 | | |
| Applicant TUFTS UNIVERSITY | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|---|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35 | Date of issuance of this report 08 December 2005 (08.12.2005) Authorized officer <div style="text-align: center; font-weight: bold;">Masashi Honda</div> Telephone No. +41 22 338 70 10 |
|---|---|

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/00255

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/00255

Box No. II Priority

1. ☐ The following document has not yet been furnished:
 - ☐ copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority has been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

This International Searching Authority acknowledges applicant's claim for priority to U.S. Provisional Application Number 60/438,393 files 07 January 2003.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/00255

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>1-59</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive step (IS) | Claims <u>1-59</u> | YES |
| | Claims <u>NONE</u> | NO |
| Industrial applicability (IA) | Claims <u>1-59</u> | YES |
| | Claims <u>NONE</u> | NO |

2. Citations and explanations:

Claims 1-59 meet the criteria set out in PCT Articles 33 (2)-(4), because the cited prior art references do not specifically teach a composition comprising porous silk fibroin material having all the properties (e.g., a compressive modulus of at least 100 kPa or a pore diameter of 10-1000 microns with a biologically or pharmaceutically active molecule, i.e., a growth factor, cytokine or integrin) as claimed instantly. The cited prior art further does not teach a method to make said silk fibroin material or said material comprising a biocompatible material. The cited art also does not teach methods to produce an engineered tissue, a cartilaginous tissue comprising seeding multiple mammalian cells or a to produce a bone tissue according to the steps and components claimed in said method (s). The cited prior art references only refer to the subject matter of the claimed invention in general terms with only specificity that the silk fibroin is applicable in the composition and methods cited in said prior art references.

Thus, the cited references do not teach or reasonably suggest compositions or methods to obtain the claimed invention. Therefore, the Claimed invention is neither anticipated nor lacks an inventive step over the cited prior art and thus has industrial applicability because the subject matter claimed can be made or used in industry.